ORIGINAL ARTICLE

Trial of Endovascular Treatment of Acute Basilar-Artery Occlusion

C. Tao, R.G. Nogueira, Y. Zhu, J. Sun, H. Han, G. Yuan, C. Wen, P. Zhou, W. Chen, G. Zeng, Y. Li, Z. Ma, C. Yu, J. Su, Z. Zhou, Z. Chen, G. Liao, Y. Sun, Y. Ren, H. Zhang, J. Chen, X. Yue, G. Xiao, Li Wang, R. Liu, W. Liu, Y. Liu, Li Wang, C. Zhang, T. Liu, J. Song, R. Li, P. Xu, Y. Yin, G. Wang, B. Baxter, A.I. Qureshi, X. Liu, and W. Hu, for the ATTENTION Investigators*

ABSTRACT

BACKGROUND

Data from trials investigating the effects and risks of endovascular thrombectomy for the treatment of stroke due to basilar-artery occlusion are limited.

METHODS

We conducted a multicenter, prospective, randomized, controlled trial of endovascular thrombectomy for basilar-artery occlusion at 36 centers in China. Patients were assigned, in a 2:1 ratio, within 12 hours after the estimated time of basilar-artery occlusion to receive endovascular thrombectomy or best medical care (control). The primary outcome was good functional status, defined as a score of 0 to 3 on the modified Rankin scale (range, 0 [no symptoms] to 6 [death]), at 90 days. Secondary outcomes included a modified Rankin scale score of 0 to 2, distribution across the modified Rankin scale score categories, and quality of life. Safety outcomes included symptomatic intracranial hemorrhage at 24 to 72 hours, 90-day mortality, and procedural complications.

RESULTS

Of the 507 patients who underwent screening, 340 were in the intention-to-treat population, with 226 assigned to the thrombectomy group and 114 to the control group. Intravenous thrombolysis was used in 31% of the patients in the thrombectomy group and in 34% of those in the control group. Good functional status at 90 days occurred in 104 patients (46%) in the thrombectomy group and in 26 (23%) in the control group (adjusted rate ratio, 2.06; 95% confidence interval [CI], 1.46 to 2.91, P<0.001). Symptomatic intracranial hemorrhage occurred in 12 patients (5%) in the thrombectomy group and in none in the control group. Results for the secondary clinical and imaging outcomes were generally in the same direction as those for the primary outcome. Mortality at 90 days was 37% in the thrombectomy group and 55% in the control group (adjusted risk ratio, 0.66; 95% CI, 0.52 to 0.82). Procedural complications occurred in 14% of the patients in the thrombectomy group, including one death due to arterial perforation.

CONCLUSIONS

In a trial involving Chinese patients with basilar-artery occlusion, approximately one third of whom received intravenous thrombolysis, endovascular thrombectomy within 12 hours after stroke onset led to better functional outcomes at 90 days than best medical care but was associated with procedural complications and intracerebral hemorrhage. (Funded by the Program for Innovative Research Team of the First Affiliated Hospital of USTC and others; ATTENTION ClinicalTrials.gov number, NCT04751708.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Hu can be contacted at andinghu@126.com or at the Stroke Center and Department of Neurology, First Affiliated Hospital of USTC, 17 Lujiang Rd., Hefei 230001, China.

*A list of the investigators in the ATTENTION trial is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Tao, Nogueira, Zhu, and Han, and Drs. X. Liu and Hu, contributed equally to this article.

ORCID information for Dr. Li Wang of Zigong Third People's Hospital, Zigong, and for Dr. Li Wang of the First Affiliated Hospital of USTC, Hefei, is available at https://orcid.org/0000-0002-6484-9324 and https://orcid.org/0000-0002-0528-7835, respectively.

N Engl J Med 2022;387:1361-72.
DOI: 10.1056/NEJMoa2206317

A Quick Take is available at NEJM.org

Among patients with basilar-artery occlusion who present with moderate-to-severe clinical findings, up to 80% die or remain with severe disability despite best medical care.[1-3] Endovascular thrombectomy has become a standard treatment for acute large-vessel-occlusion strokes involving the anterior circulation within certain time constraints.[4,5] However, there is limited evidence to support the use of endovascular thrombectomy in patients with acute basilar-artery occlusion.

Two randomized trials, the Endovascular Treatment versus Standard Medical Treatment for Vertebrobasilar Artery Occlusion (BEST) trial and the Basilar Artery International Cooperation Study (BASICS), investigated the safety and efficacy of endovascular thrombectomy in patients with basilar-artery occlusion.[6,7] Despite numerical differences in favor of endovascular thrombectomy, these trials did not show the superiority of endovascular thrombectomy plus best medical care over best medical care alone. However, there were high rates of crossovers in the BEST trial and a lack of consecutive enrollment in BASICS, which limited the certainty of their results. Previous observational studies and meta-analyses have also shown mixed results regarding the association of endovascular thrombectomy and clinical outcomes in patients with basilar-artery occlusion.[1-3,8-13] We undertook the Endovascular Treatment for Acute Basilar-Artery Occlusion (ATTENTION) trial to investigate whether endovascular thrombectomy added to best medical care would be superior to best medical care alone in patients with acute stroke due to basilar-artery occlusion who presented within 12 hours after the estimated time of basilar-artery occlusion.

METHODS

TRIAL DESIGN AND OVERSIGHT

We conducted this investigator-initiated, multicenter, prospective, randomized, open-label trial at 36 centers in China (Fig. S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). The trial protocol, available at NEJM.org, was approved by the medical ethics committee of the First Affiliated Hospital of the University of Science and Technology of China and all relevant local ethics committees. Written informed consent was obtained before randomization from all the patients or their legal representatives. The trial was performed in accordance with the principles of the Declaration of Helsinki as amended. Details of the trial rationale, design, and methods are provided in the protocol.

The steering committee designed the trial and oversaw its conduct and the data analysis. An independent data and safety monitoring board was responsible for the safety, ethics, and oversight of the trial. An independent clinical research organization (JetMed) was involved in monitoring trial quality. An independent clinical-event adjudication committee, whose members were unaware of the trial-group assignments, adjudicated the primary and secondary efficacy outcomes. An independent adverse-events committee assessed adverse events, procedural-related complications, and serious adverse events. All the images were assessed in a blinded manner by a central imaging laboratory. An independent statistician was responsible for the statistical analysis. The methods of this trial have been published previously.[14]

The trial was funded by the Program for Innovative Research Team of the First Affiliated Hospital of the University of Science and Technology of China, the Beijing Dingyi Foundation (China Special Fund for Stroke Prevention and Treatment), and the Beijing Healthunion Cardio-Cerebrovascular Disease Prevention and Treatment Foundation. These entities were not involved in the design or conduct of the trial or the decision to submit the manuscript for publication. Members of the executive committee collected the data and made the decision to submit the manuscript for publication. The first draft of the manuscript was written by the first author, and all the authors contributed to critical review of the manuscript. The authors vouch for the accuracy and completeness of the presented data, for the fidelity of the trial to the protocol, and for the accurate reporting of adverse events.

PATIENTS AND PARTICIPATING CENTERS

Patients were eligible for enrollment if they were 18 years of age or older and had had a moderate-to-severe acute ischemic stroke consistent with basilar-artery occlusion. A moderate-to-severe acute ischemic stroke was defined by a score of

10 or higher on the National Institutes of Health Stroke Scale (NIHSS; range, 0 to 42, with higher scores indicating greater neurologic deficits) at the time of neuroimaging. Basilar-artery occlusion was confirmed on computed tomographic (CT) angiography (CTA), magnetic resonance angiography (MRA), or digital subtraction angiography within 12 hours after the estimated time of stroke onset. The estimated time at which occlusion occurred was defined as the time of sudden onset of basilar-artery stroke symptoms, with no consideration of any preceding minor prodromal symptoms, as adjudicated by two neurologists. For patients whose stroke was evident on awakening or who had an unwitnessed time of stroke onset because of unconsciousness, a 12-hour time window was calculated from the time at which the patient was last seen to be well. Imaging to determine whether a patient fulfilled the enrollment criteria was done mostly at the trial hospitals, even if imaging had been previously performed at another institution. Patients who had basilar-artery occlusion that was observed at a referring hospital but who were found to have a patent artery at the trial hospital were not enrolled.

Patients were excluded if they had prestroke score, assessed retrospectively, of at least 3 on the modified Rankin scale (range, 0 to 6, with a score of 0 indicating no disability, 1 no clinically significant disability, 2 slight disability, 3 moderate disability but remaining able to walk unassisted, 4 moderately severe disability, 5 severe disability, and 6 death) among those younger than 80 years of age or a modified Rankin scale score of at least 1 among those 80 years of age or older; if they had intracranial hemorrhage on neuroimaging; or if they had a posterior circulation Alberta Stroke Program Early Computed Tomography Score (PC-ASPECTS) of less than 6 points among patients younger than 80 years of age and of less than 8 points among those 80 years of age or older.[15] The PC-ASPECTS is a 10-point imaging scoring system to quantify early ischemic changes in the posterior circulation territory, with a score of 10 indicating normal appearance and 1 point subtracted for each abnormal region on noncontrast CT or CTA source images or on diffusion-weighted magnetic resonance imaging (with lower scores indicating a larger territory of ischemic change). The full inclusion and exclusion criteria are listed in the protocol.

Centers were eligible to participate in the trial if more than 100 endovascular thrombectomy procedures for acute ischemic stroke had been completed there in the year 2020, if the center had a mean time of less than 60 minutes from hospital arrival to the start of intravenous thrombolysis, and if the center had a time of less than 90 minutes from hospital arrival to arterial puncture. Interventional operators must have had more than 5 years of experience in cerebrovascular interventional therapy and must have independently completed more than 80 thrombectomy procedures. The number of endovascular procedures that were performed in 2021 and the number of beds in each center are listed in Table S1.

Participating centers were instructed to keep a screening log of all the patients who presented with suspected basilar-artery occlusion and were thought to potentially qualify for the trial. Centers were instructed to specify patients who were eligible to participate in the trial but were not enrolled, as well as those who were not eligible to participate after additional screening.

TRIAL DESIGN

Patients were randomly assigned in a 2:1 ratio to undergo endovascular thrombectomy and receive best medical care (thrombectomy group) or to receive best medical care alone (control group). Randomization was performed as soon as possible after the occlusion of the basilar artery had been confirmed on imaging at trial hospitals and written informed consent for trial participation had been obtained. Owing to the nature of the intervention, treatment assignments were not concealed from patients or the treating team. The randomization procedure was Web-based on mobile devices or webpage platforms.

TREATMENTS

Patients in each treatment group received what was considered to be best medical care, including intravenous thrombolytic agents, antiplatelet drugs, anticoagulation, or combinations of these treatments according to national and institutional guidelines. The standard care for acute basilar-artery occlusion in China is that patients

arriving at a hospital within 4.5 hours after stroke onset receive intravenous thrombolysis. Most patients were required to pay for the thrombolytic drugs in advance, and some were eligible for reimbursement from government insurance. The strategies that were used for endovascular treatment included stent retrievers, thromboaspiration, balloon angioplasty, stent deployment, intraarterial thrombolysis (with alteplase or urokinase), or combinations of these approaches that were left to the discretion of the treating team.

OUTCOMES

The primary outcome was good functional status, defined as a modified Rankin scale score of 0 to 3, at 90 days (within a window of ±14 days). Secondary efficacy outcomes included excellent functional outcome, defined as a modified Rankin scale score of 0 to 2, at 90 days (window, ±14 days); the distribution of modified Rankin scale scores toward a better outcome at 90 days (window, ±14 days); the NIHSS score at 24 to 72 hours and at 5 to 7 days or discharge (whichever came first); the score on the European Quality of Life 5-Dimension 5-Level (EQ-5D-5L) patient-reported questionnaire (range, −0.39 to 1, with higher scores indicating a better quality of life); and the Barthel Index (dichotomized as 0 to 94 vs. 95 to 100, with a score of 95 to 100 indicating no interference with daily activities).[16] The modified Rankin scale scores at 90 days were obtained by means of a structured telephone interview that was performed by local certified neurologists or nurses who were unaware of the trial-group assignments.

Safety outcomes included symptomatic intracranial hemorrhage according to the modified Safe Implementation of Thrombolysis in Stroke–Monitoring Study (SITS-MOST) criteria, defined as local or remote parenchymal hemorrhage type 2, subarachnoid hemorrhage, or intraventricular hemorrhage that led to death or was observed on an imaging scan obtained 24 to 72 hours after treatment, combined with a neurologic deterioration of at least 4 points from baseline on the NIHSS or from the lowest NIHSS score between baseline and 24 hours, or death from any cause within 90 days (window, ±14 days).[17] Imaging outcomes included intracranial hemorrhage according to the Heidelberg classification and recanalization on CTA or MRA at 24 to 72 hours (modified Arterial Occlusive Lesion score of 2 to 3, on a scale from 0 [no recanalization] to 3 [complete recanalization]).[18]

STATISTICAL ANALYSIS

On the basis of BEST trial, we originally calculated that the enrollment of 192 patients would provide the trial with 80% power to detect a between-group difference of 20 percentage points in the percentage of patients with good functional status at 90 days (primary outcome; 25% in the control group vs. 45% in thrombectomy group) at a two-sided significance level of 0.05.[6] After the results of BASICS became available, the steering committee revised the sample size to 342 on the basis of the combined results of the BEST and BASICS trials (new estimate, 25% in the control group vs. 40% in thrombectomy group, with a 15-percentage-point difference),[6,7] with allowance for 5% of the patients to be lost to follow-up or have data that could not be evaluated.

The primary analysis was performed in the intention-to-treat population, which included all the patients who provided informed consent and underwent randomization. Supportive analyses of the primary outcome were performed in the per-protocol population, which excluded patients who did not meet the inclusion or exclusion criteria or who crossed over to the other treatment group.

We compared the results for the primary, secondary, and safety outcomes between patients undergoing endovascular thrombectomy and those receiving best medical care in multivariable logistic and linear regressions with adjustment for age, modified Rankin scale score before the stroke, time from stroke onset to randomization, and baseline stroke severity (NIHSS score). Adjusted rate ratios or risk ratios with 95% confidence intervals were reported for dichotomous outcomes.[19] The shift of the modified Rankin scale scores toward a better functional outcome was estimated with an ordinal logistic-regression model after verification of the proportional-odds assumption by the Brant test. For the comparison of the two treatment groups with respect to the secondary outcomes of the NIHSS and EQ-5D-5L scores at 90 days (modeled as continuous variables), linear regression was

used to calculate the beta coefficient. Subgroup analyses were prespecified for the primary outcome according to sex (male or female), age (<70 years or ≥70 years and <80 years or ≥80 years), baseline stroke severity (NIHSS score 10 to 19 or ≥20), time from the estimated time of basilar-artery occlusion to randomization (<6 hours or ≥6 hours), intravenous thrombolysis (no or yes), location of basilar-artery occlusion (proximal, middle, or distal), the presumed cause of the basilar-artery occlusion (large-artery atherosclerosis, cardioembolism, or undetermined and other determined cause), intracranial atherosclerotic disease as cause of stroke (yes or no), and PC-ASPECTS at baseline (<8 or ≥8).

Because the statistical plan did not include a provision for the correction of the widths of confidence intervals for multiple comparisons, no definite conclusions can be drawn from secondary-outcome results or subgroup analyses. No imputations for missing data were performed. All the analyses were performed with the use of Stata software, version 17.0 (StataCorp).

RESULTS

PATIENTS

From February 21, 2021, through January 3, 2022, a total of 507 patients were assessed for participation in the trial, of whom 141 did not meet the eligibility criteria (5 patients had a spontaneous recanalization before randomization) and 24 declined to participate. The remaining 342 patients were randomly assigned to a treatment group; 228 to the thrombectomy group and 114 to the control group (Fig. 1). The legal representatives of 2 patients who had been assigned to the thrombectomy group withdrew their consent, so 340 patients were included in the intention-to-treat analysis.

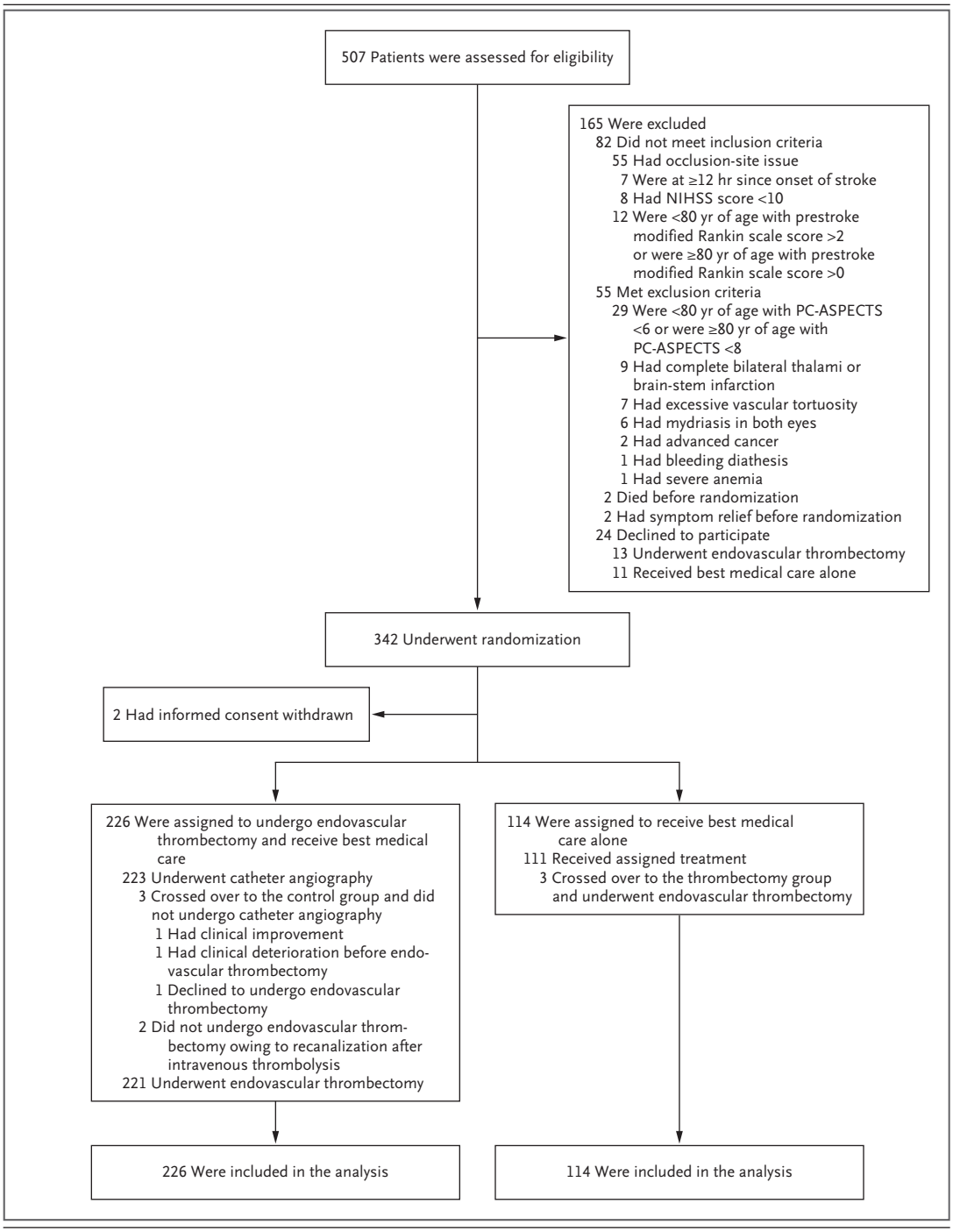
The demographic and clinical characteristics of the patients at baseline were similar in the two groups, as shown in Table 1 and Table S2; these tables also show data on additional procedural characteristics and workflow measures. The representativeness of the enrolled patients is summarized in Table S3. Intravenous thrombolysis was administered in 31% of the patients in the thrombectomy group and in 34% of those in the control group. Details of the endovascular thrombectomy procedures are described in Table S4. The mean age of the patients was 66 years in the thrombectomy group and 67 years in the control group. The median estimated time from basilar-artery occlusion to randomization was 5.1 hours in the thrombectomy group and 4.9 hours in the control group. The median NIHSS score at the time of the baseline examination at the trial hospital was 24 in each group. The median PC-ASPECTS was 9 in the thrombectomy group and 10 in the control group. A total of 183 patients completed neuroimaging within less than 4.5 hours after the estimated time of basilar-artery occlusion; of these, 103 patients (56%) received intravenous thrombolysis, and the percentages were similar in the two trial groups.

Six patients (3 in the thrombectomy group and 3 in the control group) crossed over to receive the other therapy. Two patients in the thrombectomy group underwent diagnostic angiography only, owing to complete recanalization after intravenous thrombolysis. Therefore, 221 patients in the thrombectomy group underwent endovascular thrombectomy. General anesthesia was used in 124 of 223 patients (56%). A total of 40% of the patients underwent additional intracranial angioplasty or stenting, and 8% underwent extracranial angioplasty or stenting.

The clinical event-adjudication committee and imaging-evaluation committee excluded 12 patients from the per-protocol analysis, including the 6 patients who crossed over to the other group, 2 who underwent randomization more than 12 hours after the estimated time of basilar-artery occlusion, 2 who had a PC-ASPECTS of less than 6 points, 1 who had a PC-ASPECTS of less than 8 points and was older than 80 years of age, and 1 in whom the basilar artery was considered to be occluded by the treating team but was found to be critically stenotic by the imaging core laboratory (Table S5). No patients were lost to follow-up or had data missing for main baseline covariates and primary outcome.

PRIMARY AND SECONDARY OUTCOMES

Good functional status at 90 days (modified Rankin scale score, 0 to 3; the primary outcome) was observed in 46% of the patients in the thrombectomy group and in 23% of those in the control group (adjusted rate ratio, 2.06; 95% confidence interval [CI], 1.46 to 2.91; P<0.001) (Table 2). (Unadjusted values for primary and



secondary outcomes are provided in Table S6.) In the ordinal logistic-regression model to account for the shift in distribution in the modified Rankin scale score, the adjusted common odds ratio for the modified Rankin scale score toward a better outcome with endovascular thrombectomy at 90 days was 2.87 (95% CI, 1.84 to 4.47) (Fig. 2). A total of 75 patients (33%) in the thrombectomy group and 12 (11%) in the control group had excellent functional status (modified Rankin scale score, 0 to 2) at 90 days (adjusted rate ratio, 3.17; 95% CI, 1.84 to 5.46).

Figure 1 (facing page). Randomization and Treatment of the Patients.

Patients were randomly assigned in a 2:1 ratio to undergo endovascular treatment plus receive best medical care (thrombectomy group) or to receive best medical care alone (control group). Patients were required to have a score on the modified Rankin scale (range, 0 [no symptoms] to 6 [death]) of less than 3 if they were younger than 80 years of age or a score of 0 if they were 80 years of age or older. Patients were required to have a posterior circulation Alberta Stroke Program Early Computed Tomography Score (PC-ASPECTS) on noncontrast CT or CT angiographic source images or on diffusion-weighted magnetic resonance imaging of less than 6 if they were younger than 80 years of age or of less than 8 if they were 80 years of age or older. PC-ASPECTS is a 10-point imaging scoring system to quantify early ischemic changes in the posterior circulation territory, with a score of 10 indicating normal appearance and 1 point subtracted for each abnormal region (with lower scores indicating a larger territory of ischemic change).

Secondary outcomes were generally in the same direction as the primary outcome, but rate ratios were not adjusted for multiple comparisons, and no definite conclusions can be drawn from these results. Patency of the basilar artery at 24 to 72 hours as assessed on CTA or MRA was observed in 91% of the patients in the thrombectomy group and in 38% of those in the control group (Table 2). Other secondary clinical and imaging outcomes are shown in Table 2.

SAFETY

A total of 37% of the patients in the thrombectomy group and 55% of those in the control group died within 90 days (adjusted risk ratio, 0.66; 95% CI, 0.52 to 0.82). Symptomatic intracranial hemorrhage at 24 to 72 hours occurred in 12 patients (5%) in the thrombectomy group and in none of the patients in the control group. There were 32 procedural complications (in 14% of the patients in the thrombectomy group) including 6 arterial dissections and 5 vessel perforations. One patient with arterial perforation died on the day after the procedure. Other adverse events are described in Table S7, and causes of death are summarized in Table S8.

SUBGROUP AND PER-PROTOCOL ANALYSES

The results of the subgroup analyses for the primary outcome are shown in Figure 3. In the per-protocol population, the characteristics of the patients were similar in the two groups (Table S9), and the results of the analyses in the per-protocol population were generally in the same direction as those of the main analyses for the primary, secondary, and safety outcomes (Table S10 and Figs. S2 and S3).

DISCUSSION

In this trial involving patients with moderate or severe stroke due to basilar-artery occlusion who were randomly assigned to undergo endovascular thrombectomy or receive best medical care within 12 hours after the estimated time of basilar-artery occlusion, the percentage of patients with a modified Rankin scale score of 0 to 3 (good functional status) at 90 days was higher in the thrombectomy group than in the control group. Secondary outcomes generally favored the thrombectomy group, but these results were not adjusted for multiple comparisons. Mortality at 90 days was 37% in the thrombectomy group and 55% in the control group. Symptomatic intracranial hemorrhage occurred in 5% of the patients in the thrombectomy group and in none of the patients in the control group, and procedural complications, including one fatal arterial perforation, occurred in 14% of the patients in the thrombectomy group.

The ATTENTION registry that preceded this trial showed that the treatment effect of endovascular thrombectomy was modified by the NIHSS score at baseline.[3] This finding is consistent with data from both the BASICS registry and the BASICS trial, as well as from several anterior circulation trials suggesting that thrombectomy might not be beneficial in patients presenting with mild stroke.[2,7,20,21] Therefore, the steering committee decided that only patients with acute basilar-artery occlusion and an NIHSS score of at least 10 should be enrolled in this trial. Given the potential interaction between age and stroke burden with the treatment effect of endovascular thrombectomy,[22] we also opted for different thresholds for the baseline PC-ASPECTS and the prestroke modified Rankin scale score in patients younger than 80 years of age and those 80 years of age or older. Given the anticipated poor prognosis from basilar-artery occlusion, a range of 0 to 3 in the modified Rankin

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Thrombectomy (N = 226)	Control (N = 114)
Age — yr	66.0±11.1	67.3±10.2
Male sex — no. (%)	149 (66)	82 (72)
Modified Rankin scale score of 1 or 2 before stroke onset — no. (%)†	25 (11)	14 (12)
Median NIHSS score (IQR)‡	24 (15–35)	24 (14–35)
Median PC-ASPECTS (IQR)§	9 (8–10)	10 (8–10)
Cause of stroke — no. (%)¶		
Large-artery atherosclerosis	108 (48)	42 (37)
Intracranial	90 (40)	33 (29)
Extracranial	18 (8)	9 (8)
Cardioembolism	46 (20)	26 (23)
Undetermined cause	69 (31)	46 (40)
Other determined cause	3 (1)	0
Basilar-artery occlusion site — no./total no. (%)‖		
Vertebral artery V4	20/225 (9)	6/114 (5)
Proximal basilar artery	69/225 (31)	39/114 (34)
Middle basilar artery	62/225 (28)	29/114 (25)
Distal basilar artery	74/225 (33)	40/114 (35)
Intravenous thrombolysis — no. (%)**	69 (31)	39 (34)
Alteplase	60 (27)	35 (31)
Urokinase	9 (4)	4 (4)
Median duration (IQR) — hr††		
From stroke onset to randomization	5.1 (3.6–7.2)	4.9 (3.5–7.0)
From stroke onset to groin puncture	5.6 (3.5–7.5)	NA
From stroke onset to revascularization	6.9 (5.0–8.8)	NA
From groin puncture to revascularization	1.2 (0.8–1.8)	NA
Final modified TICI score of 2b or 3 — no./total no. (%)‡‡	208/223 (93)	NA

* Plus–minus values are means ±SD. IQR denotes interquartile range, and NA not applicable.
† Scores on the modified Rankin scale range from 0 (no symptoms) to 6 (death).
‡ Scores on National Institutes of Health Stroke Scale (NIHSS) range from 0 to 42, with higher scores indicating greater neurologic deficits.
§ The posterior circulation Acute Stroke Prognosis Early CT Score (PC-ASPECTS) is a 10-point grading system, with a score of 10 indicating normal and 1 point subtracted for each abnormal region.
¶ Cause of stroke was evaluated on the basis of the medical history, clinical characteristics, and imaging results.
‖ One patient was determined not to have basilar-artery occlusion.
** A total of 183 patients (120 in the thrombectomy group and 63 in the control group) had an estimated time from basilar-artery occlusion to imaging of less than 4.5 hours. Among these patients, 65 (54%) in the thrombectomy group and 38 (60%) in the control group received intravenous thrombolysis. A total of 94 of 152 patients (59 of 99 in the thrombectomy group and 35 of 53 in the control group) who had an estimated time from basilar-artery occlusion to imaging of less than 3.5 hours received intravenous thrombolysis.
†† Onset denotes the estimated time of basilar-artery occlusion.
‡‡ The modified Thrombolysis in Cerebral Infarction (TICI) scale ranges from 0 (no reperfusion) to 3 (full reperfusion in the distribution of the occluded artery).

Table 2. Outcomes According to Assigned Treatment Group.*

Outcome	Thrombectomy (N = 226)	Control (N =114)	Measure of Effect	Adjusted Value of Effect (95% CI)†
Primary outcome				
Modified Rankin scale score of 0–3 at 90 days — no. (%)	104 (46)	26 (23)	Rate ratio	2.06 (1.46 to 2.91)
Secondary clinical outcomes				
Median distribution across the modified Rankin scale categories (IQR)	4 (2 to 6)	6 (4 to 6)	Common odds ratio	2.87 (1.84 to 4.47)
Modified Rankin scale score of 0 to 2 at 90 days — no. (%)	75 (33)	12 (11)	Rate ratio	3.17 (1.84 to 5.46)
Median NIHSS score (IQR)‡				
At 24–72 hr	21 (7 to 35)	30 (15 to 38)	Beta coefficient	–5.94 (–8.71 to –3.18)
At 5–7 days or discharge	16 (4 to 36)	35 (11 to 41)	Beta coefficient	–8.64 (–12.01 to –5.27)
Barthel Index of 95 or 100 at 90 days — no. (%)§	77 (34)	15 (13)	Rate ratio	2.60 (1.60 to 4.21)
Median EQ-5D-5L score at 90 days (IQR)¶	0.12 (0 to 0.89)	0 (0 to 0.12)	Beta coefficient	0.25 (0.15 to 0.34)
Secondary imaging outcomes				
Patency at 24–72 hr on CTA or MRA — no./total no. (%)‖	147/161 (91)	26/69 (38)	Rate ratio	2.58 (1.89 to 3.51)
Intracranial hemorrhage at 24–72 hr as assessed radiologically — no. (%)	31 (14)	2 (2)	Risk ratio	8.13 (1.98 to 33.4)
Safety outcomes				
Death within 90 days — no. (%)	83 (37)	63 (55)	Risk ratio	0.66 (0.52 to 0.82)
Death within 7 days — no. (%)	57 (25)	38 (33)	Risk ratio	0.75 (0.54 to 1.04)
Symptomatic intracranial hemorrhage according to SITS-MOST criteria at 24–72 hr — no. (%)**	12 (5)	0	—	NE

* CTA denotes computed tomographic angiography, MRA magnetic resonance angiography, and NE not estimated.

† Estimates were adjusted for age, for the modified Rankin scale score before stroke onset, the time from onset to randomization, and stroke severity (according to the NIHSS score). The widths of confidence intervals for difference or risks for secondary outcomes were not adjusted for multiple comparisons, and no conclusions can be drawn from these data.

‡ NIHSS scores at 24 hours were not available for 24 patients: 21 died before assessment, and 3 had missing scores. The score at 5 to 7 days or discharge (whichever came first) was not available for 81 patients: 65 died before assessment, and 16 had missing scores. According to the statistical analysis plan, the worst score was assigned for patients who had died.

§ The Barthel Index is an ordinal scale for measuring performance of patients' self-care activities of daily living. Scores range from 0 to 100, with 0 indicating severe disability and 95 or 100 indicating no disability that interferes with daily activities. According to the statistical analysis plan, the worst score was assigned for patients who had died.

¶ The European Quality of Life Group 5-Dimension 5-Level (EQ-5D-5L) patient-reported questionnaire is a standardized instrument for the measurement of health status. Scores range from –0.39 to 1.00, with higher scores indicating better quality of life. A score of 0 is the value of a health state equivalent to death, with negative values being worse than death and 1 is full health.

‖ Patency was defined as a score of 2 or 3 on the modified Arterial Occlusive Lesion scale, which ranges from 0 (complete occlusion) to 3 (complete recanalization and restoration of the target artery). Data on follow-up CTA or MRA were not available because of serious illness or death in 110 patients.

** Symptomatic intracranial hemorrhage was evaluated by an adverse-event committee according to the Safe Implementation of Thrombolysis in Stroke–Monitoring Study (SITS-MOST) criteria, defined as local or remote parenchymal hemorrhage type 2, subarachnoid hemorrhage, or intraventricular hemorrhage that led to death or was observed on an imaging scan obtained 24 to 72 hours after treatment, combined with a neurologic worsening of at least 4 points from baseline on the NIHSS or from the lowest NIHSS score between baseline and 24 hours, or death from any cause within 90 days (window, ±14 days).[17]

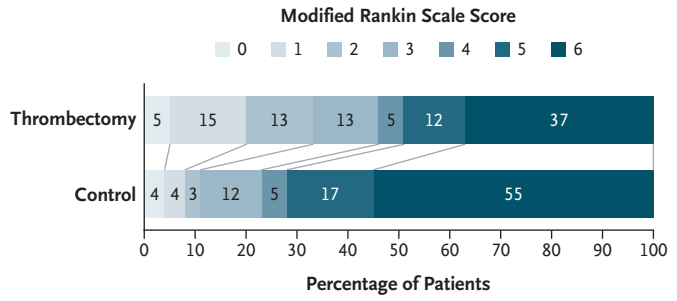


Figure 2. Distribution of Functional Outcomes at 90 Days in the Intention-to-Treat Population.

Shown are scores on the modified Rankin scale for the patients in the two treatment groups. The intention-to-treat population included all the patients who provided informed consent and underwent randomization. No patients were lost to follow-up. Scores range from 0 to 6, with 0 indicating no symptoms, 1 no clinically significant disability, 2 slight disability (patients are able to look after their own affairs without assistance but are unable to carry out all previous activities), 3 moderate disability (patients require some help but are able to walk unassisted), 4 moderately severe disability (patients are unable to attend to bodily needs without assistance and are unable to walk unassisted), 5 severe disability (patients require constant nursing care and attention), and 6 death. The adjusted common odds ratio for the modified Rankin scale score toward a better outcome with endovascular thrombectomy at 90 days was 2.87 (95% CI, 1.84 to 4.47).

scale score (with a score of 3 indicating moderate disability requiring assistance but retaining an ability to walk) rather than a range of 0 to 2 was used as the primary outcome, which is the same as the outcome chosen in the BEST and BASICS trials.[6,7]

The percentages of patients with symptomatic intracranial hemorrhage after endovascular thrombectomy of basilar-artery occlusion are relatively consistent across trials (approximately 4 to 8%)[6,7]; the percentage has been approximately 4% in anterior circulation trials of endovascular treatment.[4] However, most trials have shown no symptomatic intracranial hemorrhages in patients with basilar-artery occlusion who did not undergo thrombectomy, and so the percentage is lower than for anterior circulation stroke.[4,6,7] This situation suggests that the added risk of symptomatic intracranial hemorrhage with thrombectomy may be higher among patients with basilar-artery occlusion than among those with anterior circulation strokes. In our trial, intracranial hemorrhage occurred in approximately 5% of the patients who underwent thrombectomy, and no patient in the control group had intracranial hemorrhage.

Limitations of our trial include the exclusive enrollment of Chinese patients, who have a high prevalence of intracranial large-artery atherosclerosis, and our results may not be generalizable to Western countries. The cause of stroke was large-artery atherosclerosis in approximately 44% of the patients in the trial, which led to high rates of intracranial or extracranial angioplasty or stenting. Angioplasty and stenting are technically demanding procedures and may be associated with higher complication rates than mechanical thrombectomy alone. Our results are not generalizable to patients with milder stroke (NIHSS score, <10) or to those who present beyond 12 hours after the estimated time of basilar-artery occlusion. The Basilar Artery Occlusion Chinese Endovascular (BAOCHE) trial, the results of which are published in this issue of the *Journal*,[23] assessed the efficacy of endovascular thrombectomy 6 to 24 hours after basilar-artery occlusion and may provide information about the effect of endovascular thrombectomy in patients with longer times to hospital arrival than were included in our trial. Approximately one third of the patients in each group in our trial received intravenous thrombolysis, as compared with approximately 80% of the patients in BASICS, which may have disadvantaged the control group in our trial. This difference may be related to the fact that during the first 4 years of recruitment, BASICS required all patients to be eligible for intravenous thrombolysis. Furthermore, that trial used a 6-hour time window for intravenous thrombolysis, as compared with the 12-hour window that was used in ATTENTION. Finally, most patients in China are required to pay in advance for intravenous thrombolysis, and this disincentive, although similarly present in the two trial groups, may have led to the relatively low use of intravenous thrombolysis and contributed to a poorer outcome in the control group. However, despite more than three quarters of the patients receiving intravenous thrombolysis in BASICS, a modified Rankin scale score of 0 to 3 was observed in essentially the same percentage of patients in the medical care group in that trial as in our trial.

Among patients with moderate or severe stroke symptoms who presented within 12 hours

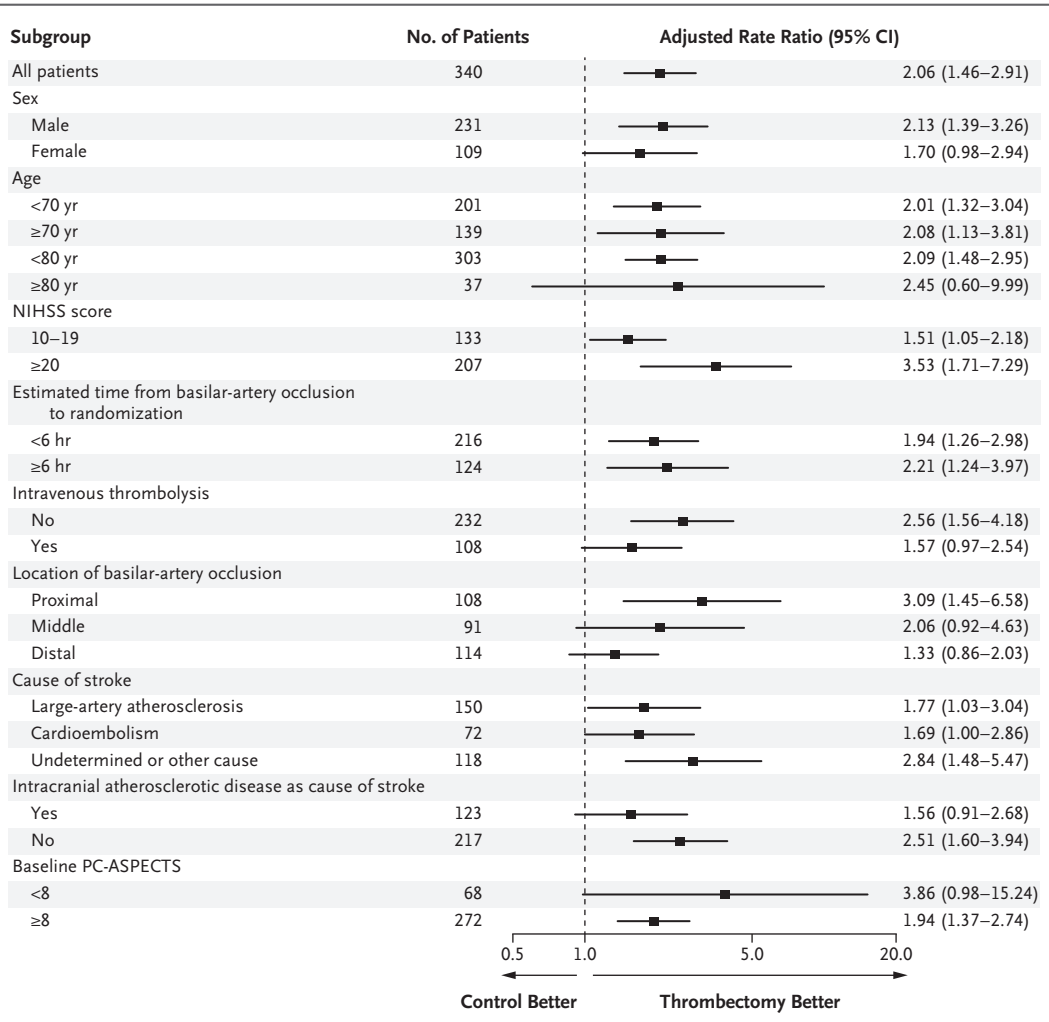


Figure 3. Subgroup Analyses of a Modified Rankin Scale Score of 0 to 3 at 90 Days (Primary Outcome).

Scores on the National Institutes of Health Stroke Scale (NIHSS) range from 0 to 42, with higher scores indicating greater neurologic deficits. The trial was not powered and had no prespecified correction for multiple comparisons for a definitive analysis of subgroups.

after basilar-artery occlusion, approximately one third of whom received intravenous thrombolysis, endovascular thrombectomy was superior to best medical care alone with respect to good functional status at 90 days. However, endovascular thrombectomy was associated with more intracerebral hemorrhages and with procedural complications.

Supported by the Program for Innovative Research Team of the First Affiliated Hospital of the University of Science and Technology of China, the Beijing Dingyi Foundation (China Special Fund for Stroke Prevention and Treatment), and the Beijing Healthunion Cardio-Cerebrovascular Disease Prevention and Treatment Foundation.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

APPENDIX

The authors' full names and academic degrees are as follows: Chunrong Tao, M.D., Ph.D., Raul G. Nogueira, M.D., Yuyou Zhu, M.D., Jun Sun, M.D., Hongxing Han, M.D., Guangxiong Yuan, M.D., Changming Wen, M.D., Peiyang Zhou, M.D., Wenhuo Chen, M.D., Guoyong Zeng, M.D., Yuwen Li, M.D., Zhengfei Ma, M.D., Chuanqing Yu, M.D., Junfeng Su, M.D., Zhiming Zhou, M.D., Zhongjun

Chen, M.D., Geng Liao, M.D., Yaxuan Sun, M.D., Youquan Ren, M.D., Hui Zhang, M.D., Jie Chen, M.D., Xincan Yue, M.D., Guodong Xiao, M.D., Li Wang, M.D., Rui Liu, M.D., Wenhua Liu, M.D., Yong Liu, M.D., Li Wang, M.D., Chao Zhang, M.D., Tianlong Liu, M.D., Jianlong Song, M.D., Rui Li, M.D., Ph.D., Pengfei Xu, M.D., Ph.D., Yamei Yin, M.D., Guoping Wang, M.D., Blaise Baxter, M.D., Adnan I. Qureshi, M.D., Xinfeng Liu, M.D., Ph.D., and Wei Hu, M.D., Ph.D.

The authors' affiliations are as follows: the Stroke Center and Department of Neurology, First Affiliated Hospital of the University of Science and Technology of China (USTC), Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei (C.T., Y.Z., J. Sun, Li Wang, C.Z., T.L., J. Song, R. Li, P.X., Y.Y., G.W., X.L., W.H.), the Department of Neurology, Linyi People's Hospital, Linyi (H.H.), the Emergency Department, Xiangtan Central Hospital, Xiangtan (G.Y.), the Department of Neurology, Nanyang Central Hospital, Nanyang (C.W.), the Department of Neurology, Xiangyang No. 1 People's Hospital, Hubei University of Medicine, Xiangyang (P.Z.), the Department of Neurology, Zhangzhou Affiliated Hospital of Fujian Medical University, Zhangzhou (W.C.), the Department of Neurology, Ganzhou People's Hospital, Ganzhou (G.Z.), the Department of Neurology, Heze Municipal Hospital, Heze (Y. Li), the Department of Neurology, Suzhou Hospital of Anhui Medical University (Z.M.), and the Department of Neurology and Clinical Research Center of Neurologic Disease, Second Affiliated Hospital of Soochow University (G.X.), Suzhou, the Department of Neurology, First Affiliated Hospital of Anhui University of Science and Technology, First People's Hospital of Huainan, Huainan (C.Y.), the Department of Neurology, Jingzhou Hospital Affiliated to Yangtze University, Jingzhou (J. Su), the Department of Neurology, Yijishan Hospital of Wannan Medical College, Wuhu (Z.Z.), the Department of Neurointervention, Dalian Municipal Central Hospital Affiliated with Dalian Medical University, Dalian (Z.C.), the Department of Neurology, Maoming People's Hospital, Maoming (G.L.), the Department of Neurology, Shanxi Provincial People's Hospital, Taiyuan (Y.S.), the Department of Neurology, Linquan Country People's Hospital, Linquan (Y.R.), the Department of Neurosurgery, Second Affiliated Hospital of Bengbu Medical College, Bengbu (H.Z.), the Department of Neurosurgery, Tongling People's Hospital, Tongling (J.C.), the Department of Neurosurgery, Zhoukou Central Hospital of Henan University, Zhoukou (X.Y.), the Department of Neurology, Zigong Third People's Hospital, Zigong (Li Wang), the Department of Neurology, Affiliated Jinling Hospital, Medical School of Nanjing University, Nanjing (R. Liu, X.L.), the Department of Neurology, Wuhan No. 1 Hospital, Wuhan (W.L.), and the Department of Neurology, Lu'an Hospital of Anhui Medical University, Lu'an (Y. Liu) — all in China; the UPMC Stroke Institute, Department of Neurology and Neurosurgery, University of Pittsburgh School of Medicine, Pittsburgh (R.G.N.), and Lehigh Valley Health Network, Allentown (B.B.) — both in Pennsylvania; and the Zeenat Qureshi Stroke Institute and Department of Neurology, University of Missouri, Columbia (A.I.Q.).

REFERENCES

1. Writing Group for the BASILAR Group. Assessment of endovascular treatment for acute basilar artery occlusion via a nationwide prospective registry. JAMA Neurol 2020;77:561-73.
2. Schonewille WJ, Wijman CAC, Michel P, et al. Treatment and outcomes of acute basilar artery occlusion in the Basilar Artery International Cooperation Study (BASICS): a prospective registry study. Lancet Neurol 2009;8:724-30.
3. Tao C, Qureshi AI, Yin Y, et al. Endovascular treatment versus best medical management in acute basilar artery occlusion strokes: results from the ATTENTION multicenter registry. Circulation 2022;146:6-17.
4. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet 2016;387:1723-31.
5. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2019;50(12):e344-e418.
6. Liu X, Dai Q, Ye R, et al. Endovascular treatment versus standard medical treatment for vertebrobasilar artery occlusion (BEST): an open-label, randomised controlled trial. Lancet Neurol 2020;19:115-22.
7. Langezaal LCM, van der Hoeven EJRJ, Mont'Alverne FJA, et al. Endovascular therapy for stroke due to basilar-artery occlusion. N Engl J Med 2021;384:1910-20.
8. Gruber K, Misselwitz B, Steinmetz H, Pfeilschifter W, Bohmann FO. Evaluation of endovascular treatment for acute basilar occlusion in a state-wide prospective stroke registry. Front Neurol 2021;12:678505.
9. Katsanos AH, Safouris A, Nikolakopoulos S, et al. Endovascular treatment for basilar artery occlusion: a systematic review and meta-analysis. Eur J Neurol 2021;28:2106-10.
10. Broussalis E, Hitzl W, McCoy M, Trinka E, Killer M. Comparison of endovascular treatment versus conservative medical treatment in patients with acute basilar artery occlusion. Vasc Endovascular Surg 2013;47:429-37.
11. Mourand I, Machi P, Milhaud D, et al. Mechanical thrombectomy with the Solitaire device in acute basilar artery occlusion. J Neurointerv Surg 2014;6:200-4.
12. Seners P, Dargazanli C, Piotin M, et al. Intended bridging therapy or intravenous thrombolysis alone in minor stroke with basilar artery occlusion. Stroke 2021;52:699-702.
13. Yan S, Zhou Y, Zhao Y, et al. Effect of imaging markers on reperfusion therapy in basilar artery occlusion. Ann Neurol 2022;92:97-106.
14. Tao C, Li R, Zhu Y, et al. Endovascular treatment for acute basilar artery occlusion: a multicenter randomized controlled trial (ATTENTION). Int J Stroke 2022;17:815-9.
15. Puetz V, Khomenko A, Hill MD, et al. Extent of hypoattenuation on CT angiography source images in basilar artery occlusion: prognostic value in the Basilar Artery International Cooperation Study. Stroke 2011;42:3454-9.
16. Luo N, Liu G, Li M, Guan H, Jin X, Rand-Hendriksen K. Estimating an EQ-5D-5L value set for China. Value Health 2017;20:662-9.
17. Wahlgren N, Ahmed N, Dávalos A, et al. Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study. Lancet 2007;369:275-82.
18. von Kummer R, Broderick JP, Campbell BC, et al. The Heidelberg Bleeding Classification: classification of bleeding events after ischemic stroke and reperfusion therapy. Stroke 2015;46:2981-6.
19. Norton EC, Miller MM, Kleinman LC. Computing adjusted risk ratios and risk differences in Stata. Stata J 2013;13:492-509.
20. Goyal N, Tsivgoulis G, Malhotra K, et al. Medical management vs mechanical thrombectomy for mild strokes: an international multicenter study and systematic review and meta-analysis. JAMA Neurol 2020;77:16-24.
21. Hou X, Feng X, Wang H, Li Q. Mechanical thrombectomy for mild acute ischemic stroke with large-vessel occlusion: a systematic review and meta-analysis. Cerebrovasc Dis 2022;51:615-22.
22. Ospel JM, Kappelhof M, Kashani N, et al. Effect of age and baseline ASPECTS on outcomes in large-vessel occlusion stroke: results from the HERMES collaboration. J Neurointerv Surg 2021;13:790-3.
23. Jovin TG, Li C, Wu L, et al. Trial of thrombectomy 6 to 24 hours after stroke due to basilar-artery occlusion. N Engl J Med 2022;387:1373-84.